# Residual Solvents by Gas Chromatography/ Mass Spectrometry

## 1.0 Scope and Application

1.1 This method was adapted from the EPA Method 8260D Volatile Organic Compounds by GC/MS.

1.2 This method is used to determine residual solvents in a variety of cannabis matrices by gas chromatography mass spectrometry (GC-MS). The following solvents and decision point cutoffs have been established in WAC 314-55-102.

| Solvent | µg/g | ppm (simplified) | CAS # |
|---|---|---|---|
| Acetone | $5.0 * 10^3$ | 5000 | 67-64-1 |
| Benzene | 2.0 | 2 | 71-43-2 |
| Butanes (Sum of Isomers) | $5.0 * 10^3$ | 5000 | |
| • n-butane | | | 106-97-8 |
| • 2-methylpropane (isobutane) | | | 75-28-5 |
| Cyclohexane | $3.9 * 10^3$ | 3880 | 110-82-7 |
| Chloroform | 2.0 | 2 | 67-66-3 |
| Dichloromethane | $6.0 * 10^2$ | 600 | 75-09-2 |
| Ethanol | $5.0 * 10^3$ | 5000 | 64-17-5 |
| Ethyl acetate | $5.0 * 10^3$ | 5000 | 141-78-6 |
| Heptanes (Single Isomer) | $5.0 * 10^3$ | 5000 | |
| • n-heptane | | | 142-82-5 |
| Hexanes (Sum of Isomers) | $2.9 * 10^2$ | 290 | |
| • n-hexane | | | 110-54-3 |
| • 2-methylpentane | | | 107-83-5 |
| • 3-methylpentane | | | 96-14-0 |
| • 2,2-dimethylbutane | | | 75-83-2 |
| • 2,3-dimethylbutane | | | 79-29-8 |
| Isopropanol (2-propanol) | $5.0 * 10^3$ | 5000 | 67-63-0 |
| Methanol | $3.0 * 10^3$ | 3000 | 67-56-1 |
| Pentanes (Sum of Isomers) | $5.0 * 10^3$ | 5000 | |
| • n-pentane | | | 109-66-0 |
| • methylbutane (isopentane) | | | 78-78-4 |
| • dimethylpropane (neopentane) | | | 463-82-1 |
| Propane | $5.0 * 10^3$ | 5000 | 74-98-6 |
| Toluene | $8.9 * 10^2$ | 890 | 108-88-3 |
| Xylenes (Sum of Isomers) | $2.2 * 10^3$ | 2170 | |
| • 1,2-dimethylbenzene (ortho-) | | | 95-47-6 |
| • 1,3-dimethylbenzene (meta-) | | | 108-38-3 |
| • 1,4-dimethylbenzene (para-) | | | 106-42-3 |

1.3 This method is applicable to the analysis of other analytes should additional volatiles be added in the future.

1.4 This method is restricted for use by, or under the supervision of, analysts experienced in the use of gas chromatography mass spectrometry (GC/MS) and skilled in the interpretation of chromatography and mass spectrum results. Each analyst must demonstrate the ability to generate acceptable results with this method.

## 2.0 Summary of the Method

2.1 Volatile organic compounds (VOCs) are introduced into the GC by one of the preparation methods. The analytes may be introduced either directly through an injection port to a capillary column, or through headspace evaporating the sample before injection. The column is temperature-programmed to separate the analytes, which are then detected with a Mass Spectrometer (MS) detector interfaced to the GC.

2.2 Analytes eluted from the capillary column are introduced into the MS via a direct connection or flow splitter. Some wide-bore capillary columns may require splitting the flow prior to the MS interface, whereas narrow-bore capillary columns may be directly interfaced to the ion source or used with a restrictor column at the MS interface. Identification of target analytes is accomplished by comparing their mass spectra and retention times (RTs) with the mass spectra and RTs of known standards for the target compounds. Quantitation is accomplished by comparing the response of a major (quantitation) ion relative to an internal standard (IS) using an appropriate calibration curve for the intended application.

## 3.0 Definitions

Refer to manufacturer’s instructions for definitions that may be relevant to this procedure.

## 4.0 Interferences

4.1 In order to avoid compromising data quality, contamination of the analytical system by volatile materials from the laboratory must be reduced to the lowest practical level. Refer to each preparation method for specific guidance on QC procedures.

4.2 Volatile preparation and analysis should be physically separated from laboratory areas where target solvents are used. Air supply for the volatiles area should provide positive pressure relative to other laboratory areas. The water supply used for blanks should be isolated from target solvents and free of plastic supply piping.

4.3 Cross contamination may occur when a sample containing low concentrations of VOCs is analyzed immediately after a sample containing high concentrations of VOCs. After analysis of a sample containing high concentrations of VOCs, analysis of one or more blanks may be used to demonstrate that carryover is not a significant portion of the target response in subsequent samples.

4.4 Control of contaminants is assessed by analysis of blanks. Sample blanks provide information about the presence of contaminants at different points in the analytical process. Where measured analyte concentrations are suspected of being biased high or having false

positive results due to contamination, affected data should be qualified, and the data user should otherwise be informed of any suspected data quality issues. Subtracting blank values from sample results is not permitted.

## 5.0 Safety

There are no significant safety issues specific to this method. However, CLASP standardized methods do not purport to address all safety issues associated with their use. The laboratory is responsible for maintaining a safe work environment and a current awareness file of Occupational Safety and Health Administration (OSHA) regulations regarding the safe handling of the chemicals listed in this method. A reference file of material safety data sheets (MSDSs) must be available to all personnel involved in these analyses.

## 6.0 Equipment and Supplies

The mention of trade names or commercial products in this manual is for illustrative purposes only and does not constitute a CLASP endorsement or exclusive recommendation for use. The products and instrument settings cited in CLASP supported methods represent those products and settings used during EPA method development. Glassware, reagents, supplies, equipment, and settings other than those listed in this manual may be employed provided that method performance appropriate for the intended application has been demonstrated and documented.

6.1 Automated static headspace device.

6.2 GC/MS system

6.2.1 GC: An analytical system complete with a temperature-programmable GC suitable for splitless injection with an appropriate interface or direct split interface for sample introduction. The system includes all required accessories, including syringes, analytical columns, and gases.

6.2.1.1 The GC should be equipped with flow controllers such that the column flow rate remains constant throughout desorption and temperature program operation.

6.2.1.2 A capillary column can be directly coupled to the ion source of the MS or interfaced through a separator, depending on the size of the capillary and the requirements of the GC/MS system.

6.2.1.3 GC columns: The following columns have been found to provide good separation of VOCs:

- 30 m x 0.25 mm internal diameter (ID), 1.4-µm film thickness, DB-624 or VOCOL;
- 20 m x 0.18 mm ID, 1-µm film thickness, DB-VRX;
- 60 m x 0.32 mm ID, 1.5-µm or 1.8-µm film thickness, Rtx-Volatiles.

6.2.2 MS

6.2.2.1 Capable of acquiring mass spectra from mass/charge (m/z) 35 to 270 at a rate fast enough to acquire at least five (but preferably 10 or more) mass

spectra across each chromatographic peak of interest, using 70 volts (nominal) electron energy in the electron impact ionization mode. The MS must be capable of meeting the criteria as outlined in Sec. 11.3.

6.2.2.2 An ion trap MS may be used if it is capable of axial modulation to reduce ion-molecule reactions and can produce electron impact-like spectra that match those in the EPA/National Institute on Standards and Technology (NIST) library or equivalent. Because ion-molecule reactions with water and methanol in an ion trap MS may produce interferences that co-elute with chloromethane and chloroethane, the base peak for both of these analytes will be at m/z 49, which should also be used as the quantitation ion in this case

The MS must be capable of producing a mass spectrum which meets the criteria as outlined in Sec. 11.3.1.

6.2.2.3 A tandem MS (MS/MS) may be used if it has the necessary pumps, collision cell, collision gases, and high-vacuum system capable of performing transitions in product ion scan mode or the selected reaction monitoring mode (SRM) for the target analytes of interest. Recommendations for specific precursor and product ions in SRM are available for some target analytes from the manufacturers of the equipment. The system must be capable of documenting the performance of both MSs against manufacturer specifications for mass resolution, mass assignment, and sensitivity using the internal calibrant (e.g., perfluorotributylamine). It is recommended to check the performance of the system at least weekly or at a frequency appropriate to meet the needs of the project. At a minimum, the performance of the system must be checked just prior to the initial calibration (ICAL).

6.2.2.4 The use of a selected ion monitoring (SIM) or chemical ionization (CI) mass spectrometry are acceptable techniques for applications requiring quantitation limits below the normal range of electron impact mass spectrometry or to reduce interferences from the sample matrix.

6.2.3 GC/MS interface: One of the following examples may be used to interface the GC to the MS.

6.2.3.1 Direct coupling, by inserting the column into the MS through a heated transfer line, is generally used for capillary columns < 0.53 mm ID.

6.2.3.2 A jet separator, including an all-glass transfer line and glass enrichment device or split interface, is used with columns ≥ 0.53 mm ID.

6.2.3.3 Other interfaces may be used provided the performance specifications described in Sec. 11.3.1 are achieved.

6.2.4 Data system: A computer system that allows the continuous acquisition and storage of all mass spectra obtained throughout the duration of the chromatographic program must be interfaced to the MS. The computer must have software that allows

searching any GC/MS data file for ions of a specified mass and plotting such ion abundances versus time or scan number. This type of plot is defined as an extracted ion current profile (EICP). Software must also be available that allows integrating the abundances in any EICP between specified time or scan-number limits. A recent version of the EPA/NIST mass spectral library, or equivalent, should also be available.

6.3 Microsyringes: 10, 25, 100, 250, 500, and 1000 µL gas-tight

6.4 Syringe valve: Two-way, with Luer ends (three each), if applicable to the purging device

6.5 Syringes: 5, 10, or 25 mL, gas-tight with shutoff valve

6.6 Balance: Analytical, capable of weighing 0.0001 g, and top-loading, capable of weighing 0.1g.

6.7 Glass VOA vials: 20, 40, 60 mL, with PTFE-lined screw-top or crimp-top caps (compatible with the autosampler if appropriate for the preparation technique)

6.8 Vials: For GC autosampler

6.9 Disposable pipets: Pasteur

6.10 Volumetric flasks, Class A: 5, 10, 50, 100 mL, with ground-glass stoppers

6.11 Spatula: Stainless steel

## 7.0 Reagents and Standards

7.1 Reagent-grade chemicals must be used in all tests. Unless otherwise indicated, it is intended that all reagents conform to the specifications of the Committee on Analytical Reagents of the American Chemical Society (ACS), where such specifications are available. Other grades may be used, provided it is first ascertained that the reagent is of sufficiently high purity to permit its use without lessening the accuracy of the determination. Reagents should be stored in glass to prevent the leaching of contaminants from plastic containers.

7.2 Organic free reagent water: All references to water in this method refer to organic-free reagent water.

7.3 Hexadecane: Reagent grade, or equivalent, demonstrated to be free from interferences for the compounds of interest at the levels of interest through the analysis of a solvent blank. The results of such a blank analysis must demonstrate that no interfering volatiles are present.

7.4 Stock standard solutions: The solutions may be purchased as certified solutions or prepared from pure standard materials. Commercially prepared stock standards may be used at any concentration if they are certified by an accredited supplier or third party. Prepare stock standard solutions in a non-compound of interest solution, using assayed liquids or gases, as appropriate.

7.5 Working standards: Using stock standard solutions, prepare working standards, containing the compounds of interest, either singly or mixed together. Working standards must be stored with minimal headspace and should be checked frequently for signs of degradation or evaporation, especially just prior to preparing calibration standards. Working standards for most compounds should be replaced after four weeks unless the integrity of the standard is suspected of being compromised prior to that time. Working standards for gases should be replaced after one week unless the acceptability of the standard can be documented. When using premixed certified solutions, store according to the manufacturer's documented holding time and storage temperature recommendations.

7.6 Surrogate standards: Recommended general-use surrogates are toluene-d8, 4-bromofluorobenzene (BFB), and 1,2-dichloroethane-d4. Other compounds with physicochemical properties better resembling the analyte classes of interest may be used as surrogates (e.g., deuterated monitoring compounds in the EPA Contract Laboratory Program's (CLP) current statement of work, which can be found in Reference 14 in Sec. 16), provided they can be unambiguously identified and meet any applicable acceptance criteria described in Sec.11 for ICAL and continuing calibration verification (CCV). A stock surrogate solution should be prepared, and a surrogate standard spiking solution should be prepared from the stock at an appropriate concentration. Each sample undergoing GC/MS analysis must be spiked with the surrogate spiking solution prior to analysis.

7.7 Internal standards (IS): The recommended ISs are fluorobenzene, chlorobenzene-d5, and 1,4-dichlorobenzene-d4. Other compounds may be used as ISs as long as they have RTs similar to their target compounds, they can be unambiguously identified and meet any applicable acceptance criteria described in Sec. 11. Prepare the ISs solution in an appropriate solvent).

7.8 BFB tune verification standard: A standard solution of BFB in an appropriate solvent may be prepared for direct injection. If BFB is used as a surrogate, the surrogate solution may be used for this purpose.

7.9 Calibration standards: There are two types of calibration standards used for this method: standards made from the primary source (for ICAL and CCV) and standards made from a second source for initial calibration verification (ICV). When using premixed certified solutions, store according to the manufacturer's documented holding time and storage temperature recommendations.

7.9.1 ICAL standards must be prepared at a minimum of five different concentrations from the working dilution of stock standards or from premixed certified solutions. Prepare these solutions in organic-free reagent water or in a solvent appropriate for the specific sample preparation method used. Include a minimum of five different concentrations in the calibration for average response factor (RF) or linear (first-order) calibration models or six different concentrations for a quadratic (second-order) model, with the low standard below the cutoff or decision point. The remaining standards should correspond to the range of concentrations found in typical samples but should not exceed the working range of the GC/MS. ICAL standards should be mixed from fresh stock standards and dilution standards when generating an ICAL curve.

7.9.2 CCV standards should be prepared at a concentration near the mid- point of the ICAL from the same source as the ICAL.

7.9.3 Second source standards for ICV must be prepared using source materials from a second manufacturer or from a manufacturer's batch prepared independently from the batch used for calibration. Target analytes in the ICV are recommended to be prepared at concentrations near the mid-point of the calibration range. The standard should contain all calibrated target analytes that will be reported for the residual solvent assay.

7.9.4 All target analytes for residual solvents analysis must be included in the ICAL and CCV standard(s).

7.10 Matrix spike and LCS standards: Matrix spikes and LCSs should be prepared with target analytes from the same source as the ICAL standards to restrict the influence of accuracy on the determination of recovery throughout preparation and analysis. Include all reported target analytes in all LCS and matrix spiked samples.

7.11 Great care must be taken to maintain the integrity of all standard solutions. It is recommended that standards be stored with minimal headspace, protected from light, at ≤6 °C, or as recommended by the standard manufacturer using screw-cap or crimp-top amber containers equipped with PTFE liners. Returning standards to the refrigerator or freezer immediately after standard and sample preparation is completed will help maintain the integrity of the solutions and minimize loss of volatile target compounds. ISs and surrogates spiking solutions added by the instrument do not need to be refrigerated provided they are sealed to prevent loss.

7.12 Carrier gas: Helium or hydrogen may be used as a carrier gas. If hydrogen is used, analytical conditions may need to be adjusted for optimum performance and calibration, and all QC tests must be performed with hydrogen carrier gas. See Appendix B for guidance.

## 8.0 Sample Collection, Preservation, and Storage

Sample collection, preservation and storage requirements may vary by the specific sample type and may be specified in rules or other regulatory guidance. Where such requirements are specified in a regulation, follow those requirements. In the absence of specific regulatory requirements, use the following information as guidance in determining the sample collection, preservation, and storage requirements.

8.1 Samples should be collected in air-tight containers compatible with closed-system sample preparation and analysis techniques, if possible. Samples must be handled carefully to minimize loss of VOCs during sample collection, shipping, storage, preparation and analysis.

8.2 Samples to be analyzed for VOCs should be stored separately from standards and from other samples expected to contain significantly different concentrations of volatile compounds, or from samples collected for the analysis of other parameters such as semivolatiles.

8.3 Blanks should be used to monitor potential cross-contamination of samples due to improper handling or storage conditions. The specifics of this type of monitoring activity should be outlined in a laboratory SOP pertaining to volatiles sampling.

## 9.0 Quality Control

9.1 Each laboratory should maintain a formal quality assurance program. The laboratory should also maintain records to document the quality of the data generated. All data sheets and quality control data should be maintained for reference or inspection.

9.2 The laboratory must have QC procedures necessary to evaluate GC system operation and include evaluation of RT windows, calibration verification and chromatographic analysis of samples. In addition, discussions regarding the instrument QC categories, minimum frequency and criteria listed below can be found in the referenced sections of this method, and a summary is provided in Table 3. Quantitative sample analyses should not proceed for those analytes that do not meet the QC acceptance criteria.

9.2.1 The GC/MS tune must be verified to meet acceptance criteria prior to ICAL. Acceptance criteria are primarily intended to verify mass assignments and mass resolution under the same conditions used for analysis. See Sec. 11.3.1 for further details.

9.2.2 There must be an ICAL of the GC/MS system as described in Sec. 11.3. Prior to analyzing samples, the ICAL must be verified using a second source ICV standard, if readily available (Refer to Sec. 11.3.6).

9.2.3 Calibration of the system must be verified periodically by analysis of a CCV standard. See Sec. 11.4 for the frequency and acceptance criteria.

9.3 Method validation: Prior to implementation of a method, each laboratory must perform a full validation showing that the method performance meets expectations. If an autosampler is used to make sample dilutions, the accuracy of the dilutions should be evaluated prior to sample analysis. Whenever a significant change to instrumentation or procedure occurs, the laboratory must demonstrate that acceptable precision and bias can still be obtained. Also, whenever new staff members are trained, each analyst must show competency for the method or portion of the method for which the analyst is responsible. This demonstration should document that the new analyst is capable of successfully following the SOP established by the laboratory and meeting any applicable acceptance criteria specified therein.

9.4 Blanks

9.4.1 Before processing any samples, the analyst must demonstrate through the analysis of a method blank (MB) or instrument blank that equipment and reagents are free from contaminants and interferences. If a peak is found in the blank that would prevent the identification or bias the measurement of an analyte, the analyst should determine the source and eliminate it, if possible. As a continuing check, each time a batch of samples is analyzed, and when there is a change in reagents, a MB must be prepared and analyzed for the compounds of interest as a safeguard against chronic laboratory contamination. MBs and other blanks must be carried through all stages of sample preparation and analysis. At least one MB must be analyzed on every instrument after calibration standard(s) and prior to the analysis of any

samples. Blank(s) analyzed after a high concentration calibration standard can also be used to estimate the extent of decontamination needed to reduce the signal to an acceptable level (Sec. 9.5.2) after analyzing a sample at a similar concentration.

9.4.2 Blanks are generally considered to be acceptable if target analyte concentrations are less than one half the LOQ. Blanks may contain analyte concentrations greater than acceptance limits if the associated samples in the batch are unaffected (i.e., targets are not present in samples or sample concentrations/responses are >10X the blank).

9.4.3 If an analyte of interest is found in a sample in the batch near a concentration confirmed in the blank (refer to Sec. 9.5.2), the presence and/or concentration of that analyte should be considered suspect and may require qualification. Contaminants in the blank should meet most or all of the qualitative identifiers in Sec. 11.6 to be considered. Samples may require re-analysis if the blanks do not meet laboratory-established or project-specific criteria. Re-analysis is not necessary if the analyte concentration falls well below the cutoff or decision point.

9.4.4 When new reagents or chemicals are received, the laboratory should monitor the blanks associated with samples for any signs of contamination. It is not necessary to test every new batch of reagents or chemicals prior to sample preparation if the source/lot shows no prior problems. However, if reagents are changed during a preparation batch or a new manufacturer's lot is used, separate blanks must be prepared for each set of reagents.

9.4.5 The laboratory should not subtract the results of the MB from those of any associated samples. Such "blank subtraction" may lead to negative sample results. If the MB results do not meet acceptance criteria and reanalysis is not practical, then the data user should be provided with the sample results, the MB results, and a discussion of the corrective actions undertaken by the laboratory scientific director.

9.5 Sample QC for preparation and analysis – The laboratory must also have procedures for documenting the effect of the sample matrix on method performance (i.e., precision, bias, and method sensitivity). At a minimum, this must include the analysis of a MB, an LCS, and should include either a laboratory sample duplicate/matrix spike or matrix spike/matrix spike duplicate (where practical and sample volume is available for doing so) in each preparation batch, as well as monitoring the recovery of surrogates. These QC samples should be subjected to the same analytical procedures (Sec. 11.0) as those used on the samples.

9.5.1 A MB must be included with each analytical batch. MBs consist of an aliquot of clean (control) matrix similar to the sample and of a similar weight or volume. Other types of blanks (e.g., trip blanks, storage blanks, etc.) should be included when appropriate but are distinct from MBs.

9.5.2 An LCS must be included with each analytical batch. The LCS consists of an aliquot of a clean (control) matrix similar to the sample matrix and of the same weight or volume. The LCS is spiked with the same analytes at the same concentrations as the matrix spike, when appropriate. When the results of the matrix spike analysis indicate a potential problem due to the sample matrix itself, the LCS results are used to verify that the laboratory can perform the analysis in a clean matrix.

9.5.3 Documenting the effect of the matrix on target analyte measurements should include the analysis of at least one matrix spike and one duplicate unspiked sample or one matrix spike/matrix spike duplicate pair. If samples are expected to contain reportable levels of target analytes, then laboratories may use one matrix spike and a duplicate analysis of a non-spiked sample. If samples are not expected to contain reportable levels of target analytes, laboratories may use a matrix spike and matrix spike duplicate pair.

9.6 Surrogate recoveries: Surrogates must be added to every blank, sample, laboratory QC, and QC. The laboratory should evaluate surrogate recovery data from individual samples relative to the surrogate recovery acceptance criteria developed by the laboratory. Surrogate recovery limits for samples are 70 to 130%. Procedures for evaluating the recoveries of multiple surrogates and associated corrective actions should be defined in the laboratory's SOP.

9.7 IS responses must be monitored to ensure sensitivity is maintained and to limit the potential for measurement bias of associated target analyte concentrations. IS responses in samples are compared to responses of the same ISs in the ICAL standards or CCV standards. When IS responses fall outside the acceptance range, further investigation is warranted, and results may require qualification for detects and non-detects.

9.7.1 Documenting the effect of the matrix should include the analysis of at least one matrix spike and one duplicate unspiked sample or one matrix spike/matrix spike duplicate pair. The decision on whether to prepare and analyze duplicate samples or a matrix spike/matrix spike duplicate must be based on a knowledge of the samples in the sample batch. If samples are expected to contain target analytes, then laboratories may use one matrix spike and a duplicate analysis of an unspiked field sample. If samples are not expected to contain target analytes, laboratories should use a matrix spike and matrix spike duplicate pair.

9.7.2 A laboratory control sample (LCS) should be included with each analytical batch. The LCS consists of an aliquot of a clean (control) matrix similar to the sample matrix and of the same weight or volume. The LCS is spiked with the same analytes at the same concentrations as the matrix spike. When the results of the matrix spike analysis indicate a potential problem due to the sample matrix itself, the LCS results are used to verify that the laboratory can perform the analysis in a clean matrix.

9.8 Limit of quantitation (LOQ) – The LOQ is the lowest concentration at which the laboratory has demonstrated target analytes can be reliably measured and reported with a certain degree of confidence. The laboratory shall establish the LOQ at concentrations where both quantitative and qualitative criteria can consistently be met (see Sec. 11.6). The laboratory shall verify the LOQ at least annually and whenever significant changes are made to the preparation and/or analytical procedure, to demonstrate quantitation capability at lower analyte concentration levels. The verification is performed by the preparation and/or analysis of an LCS (or matrix spike) at 0.5 - 2 times the established LOQ. Additional LOQ verification may be useful if a matrix is expected to contain significant interferences at the LOQ. This verification may be accomplished with either clean control material or a representative sample matrix, free of target compounds. Optimally, the LOQ should be less than the desired decision level or regulatory action level based on the stated DQOs.

9.8.1 LOQ verification

9.8.1.1 The verification of LOQs using spiked clean control material represents a best-case scenario because it does not evaluate the potential matrix effects of real-world samples. For the application of LOQs with established DQOs, a representative matrix-specific LOQ verification may provide a more reliable estimate of the lower quantitation limit capabilities.

9.8.1.2 The LOQ verification is prepared by spiking a clean control material with the analyte(s) of interest at 0.5 - 2 times the LOQ concentration level(s). Alternatively, a representative sample matrix free of targets may be spiked with the analytes of interest at 0.5 - 2 times the LOQ concentration levels. This LOQ check is carried through the same preparation and analytical procedures as cannabis samples and other QC samples. LOQ verification samples must be independent from the ICAL used to calculate the target analyte concentrations (i.e. not a recalculated calibration point). It is recommended to verify the LOQ on every instrument where data is reported yearly.

9.8.1.3 Recover of target analytes in the LOQ verification should be within established in-house limits or within other such acceptance limits to demonstrate acceptable method performance at the LOQ. Until the laboratory has sufficient data to determine acceptance limits, the LCS criteria ±20% (i.e., lower limit minus 20% and upper limit plus 20%) may be used for the LOQ acceptance criteria. This practice acknowledges the potential for greater uncertainty at the low end of the calibration curve. Practical, historically based LOQ acceptance criteria should be determined once sufficient data points have been acquired.

## 10.0 Calibration and Standardization

See Secs. 11.3 and 11.4 for information on calibration and standardization.

## 11.0 Procedure

11.1 Various alternative methods are provided for sample introduction. All ISs, surrogates, and matrix spike compounds (when applicable) must be added to the samples before introduction into the GC/MS system. Consult the sample introduction method for the procedures by which to add such standards.

11.1.1 Automated static headspace: This technique may be used for the introduction of VOCs from aqueous and solid samples into the GC/MS system.

11.2 Recommended chromatographic conditions are provided as examples based on analyses performed in EPA laboratories and studies used to generate performance data for this method. The actual conditions will depend on the compounds of interest, instrument, and manufacturer's guidelines for the column selected. The maximum temperature of operation should always be verified with the specific column manufacturer.

11.2.1 General conditions

| | |
|---|---|
| Injector temperature | 200 – 275 °C |
| Transfer line temperature: | 200 – 300 °C |

11.2.2 Direct split interface: The following are example conditions:

| | |
|---|---|
| Carrier gas (He) flow rate: | 1.3 mL/min |
| Column: | 60 m x 0.25 mm ID, 1.4 µm DB-624 |
| Initial temperature: | 35 °C, hold for 3 min |
| Temperature program: | 6 °C /min to 100 °C,<br>12 °C /min to 180 °C,<br>20 °C /min to 200 °C, hold for 7 minutes |
| Inlet temperature: | 225 °C |
| Transfer line temperature: | 230 °C |
| Split ratio: | 30:1 |

11.2.3 Split injection

| | |
|---|---|
| Carrier gas (He) flow rate: | 0.9 mL/min |
| Column: | 20.0 m, 0.18 mm ID, 1.0 µm DB-VRX |
| Initial temperature: | 30 °C, hold for 3 min |
| Temperature program: | 10 °C /min to 100 °C,<br>20 °C /min to 240 °C; 1 minute hold |
| Inlet temperature: | 250 °C |
| Transfer line temperature: | 250 °C |
| Split ratio: | 50:1 |

11.2.4 Split injection

| | |
|---|---|
| Carrier gas (He) flow rate: | 0.7 mL/min |
| Column: | 20 m x 0.18 mm x 1.0 µm DB-624 |
| Initial temperature: | 40 °C, hold for 4 min |
| Temperature program: | 15 °C /min to 190 °C, Hold for 1.5 min at 250 °C |
| Split ratio: | 35:1 |

11.2.5 Direct injection

| | |
|---|---|
| Carrier gas (He) flow rate: | 4 mL/min |
| Column: | 70 m x 0.53 mm DB-624 |
| Initial temperature: | 40 °C, hold for 3 min |
| Temperature program: | 8 °C /min to 260 °C |

11.2.6 Hydrogen carrier gas

| | |
|---|---|
| Flow rate: | 1 mL/min |
| Column: | 40 m x 0.18 mm x 1-µm film thickness Rtx-VMS |
| Initial temperature: | 30 °C, hold for 4 min |
| Temperature program: | 7 °C /min to 180 °C |
| Injector temperature: | 200 °C |
| Transfer line temperature: | 200 °C |
| Split ratio: | 70:1 |

11.3 ICAL: Establish the GC/MS operating conditions, using the following as guidance:

| | |
|---|---|
| Mass range: | *m/z* of 35 – 270 |
| Acquisition rate: | To result in at least five mass spectra across the peak (but preferably ten or more) |
| Source temperature: | According to manufacturer's specifications |
| Ion trap only: | Set axial modulation, manifold temperature, and emission current to manufacturer's recommendations |

11.3.1 The GC/MS system must produce mass spectra with sufficient mass accuracy, mass resolution, and signal to be used for quantitative analysis of specific m/z ratios of ions characteristic of the target analytes, surrogates, and ISs. Standardization of MS performance also simplifies comparison of mass spectra generated on different instruments, such as by searching unknown spectra against a commercially available mass spectral library.

Acceptable system performance may also be demonstrated by meeting manufacturer specifications for mass resolution, mass accuracy, and sensitivity using the internal calibrant (e.g., Perfluorotributylamine, also known as PFTBA). Other reference compounds may also be appropriate for demonstrating acceptable MS performance depending on the system or conditions used for analysis. Regardless of how MS performance is evaluated, system calibration must not begin until performance criteria are met, and calibration standards and samples must be analyzed under the same conditions.

11.3.2 Set up the sample introduction system, and then prepare and analyze calibration standards as outlined in the preparation method of choice (see Sec. 11.1). ICAL standards must include at least five different standard concentrations for all target analytes. Surrogates may be calibrated either at multiple concentrations in the ICAL or at a single concentration (i.e., constant amount added to each calibration standard, as with IS). The base peak m/z of each target analyte and IS is appropriate for use as the primary m/z for quantitation, but another prominent m/z in the mass spectrum may also be used for quantitation provided it is used consistently. If interferences are noted at the primary m/z, use an alternate m/z. Calibration range, chromatographic performance, and extent of any carryover will depend on the introduction technique, GC column and conditions, and the tolerance of the sample introduction system and GC/MS to solvent, water, and other introduced sample matrix components.

NOTE: LOQs should be established at concentrations where both quantitative and qualitative verifications can be consistently and reliably met. Target analyte peaks in the calibration standard at the LOQ should be visually inspected to ensure that peak signal is distinguishable from background and to verify qualitative analyte identification.

11.3.3 Additional considerations for SIM and SRM analysis

SIM and SRM may be useful for applications requiring quantitation limits below the normal range of electron impact quadrupole mass spectrometry, and both are allowable options for this method. Using the primary m/z for quantitation and at least one secondary m/z for confirmation, set up the collection groups based on their

chromatographic retention times. The selected m/z values should include any mass defect noted in the target analyte mass spectra acquired on the instrument, usually less than 0.2 amu. The dwell time for each ion may be automatically calculated by the instrument software or may be calculated based on the peak widths of the analytes of interest, the number of spectra needed to be acquired across each peak, and the number of concurrent ions that need to be acquired in each segment. When fewer masses are monitored in each segment, the acquisition time for each mass can be increased, thereby increasing the sensitivity of the system. The total cycle time for the MS should be short enough that at least five, but preferably ten or more, spectra are acquired per chromatographic peak.

When compounds are analyzed in SIM or SRM mode, the following best practices are recommended:

- Monitor at least two ions for each target analyte and use the mid-point of the calibration curve to establish proper ion ratios for each compound. The ratios of primary and secondary ions are the only qualitative tool available in SIM and SRM runs (other than retention time) which increases their importance in proper identification. When interferences are expected or observed in a given matrix, acquiring multiple secondary ions may aid in qualitative identification.

- Verify that all monitored ions are correctly integrated in order to achieve proper ion ratios. Update the primary/secondary ion ratios and reference mass spectra after each ICAL using a mid-range ICAL standard.

11.3.4 Tabulate the response of the characteristic ions (see Table 1 for suggested ions) against the concentration for each target analyte and each IS. Calculate RFs for each target analyte relative to one of the ISs as follows:

$$RF = \frac{A_s \times C_{is}}{A_{is} \times C_s}$$

where:
As = Peak response of the analyte or surrogate Ais = Peak response of the IS
Cs = Concentration of the analyte or surrogate Cis= Concentration of the IS

11.3.4.1 Calculate the mean RF and the relative standard deviation (RSD) of the RFs for each target analyte using the following equations.

$$\text{mean RF} = \overline{RF} = \frac{\sum_{i=1}^{n} RF_i}{n} \qquad RSD = \frac{SD}{\overline{RF}} \times 100 \qquad SD = \sqrt{\frac{\sum_{i=1}^{n} (RF_i - \overline{RF})^2}{n-1}}$$

where:
RFi = RF for each of the calibration standards
RF = mean RF for each compound from the ICAL n = Number of calibration standards, e.g., 5
SD = Standard deviation

11.3.4.2 The RSD should be ≤20% for each target analyte. The laboratory should establish procedures in its determinative SOP (e.g., laboratory established

minimum RFs, signal to noise (S/N) checks, etc.) to ensure that the instrument is working properly and that calibration standards were correctly prepared.

NOTE: For a target analyte whose RF <0.01 (response of peak is <1/100 the response of the IS), it is recommended to increase its concentration in relation to other analytes to make the response more comparable.

11.3.5 Linearity of target analytes: If the RSD of any target analyte is ≤20%, then the RF is assumed to be constant over the calibration range, and the average RF may be used for quantitation (Sec. 11.7.2).

11.3.5.1 If the RSD of any target analyte RF is >20%, consider additional calibration options (e.g., narrowing the calibration range, changing calibration model, etc.), and apply one or more of these options in order to meet the ICAL acceptance criteria. Alternatively, the affected target analytes may be reported with an appropriate data qualifier, or the instrument may be recalibrated.

NOTE: When the RSD for the RF calibration model is >20%, plotting and visual inspection of a calibration curve can be a useful diagnostic tool. The inspection may indicate analytical problems, including errors in standard preparation, the presence of active sites in the chromatographic system, analytes that exhibit poor chromatographic behavior, etc.

NOTE: Forcing the calibration model through the origin (for analytes that are consistently detected in the laboratory reagent blanks) allows for a better estimate of the background level of blank contaminants. An accurate estimate of background contamination is necessary to set method reporting limits for method analytes when blank levels are problematic.

11.3.5.2 If more than 10% of the compounds included with the ICAL exceed the 20% RSD limit and do not meet the coefficient of determination criterion (r2≥0.995 or relative standard error (RSE) ≤20%) for alternate curve fits, then the chromatographic system is considered too imprecise for analysis to begin. Perform corrective actions as necessary (e.g., by adjusting moisture control parameters, replacing the analytical trap, column, or moisture trap, or adjusting desorb time), then repeat the calibration procedure beginning with Sec. 11.3. If compounds fail to meet these criteria, the associated concentrations may still be determined but they must be reported as estimated. In order to report non-detects, it must be demonstrated that there is adequate sensitivity to detect the failed compounds at the applicable LOQ.

11.3.5.3 Calibration, especially when using linear regression models, has the potential for a significant bias at the lower portion of the calibration curve. The lowest calibration point should be recalculated (not reanalyzed) using the final calibration curve in which this standard is used (i.e., re-fitting the response from the low concentration calibration standard back into the curve). The recalculated concentration of the low calibration point, especially where linear regression fits are used, should be within ±50% of the standard's true concentration, and the recalculated concentrations of any calibration standards above the LOQ should be within ±30%. Alternate criteria may be

applied depending on the needs of the test. However, those criteria should be clearly defined in a laboratory SOP. Analytes which do not meet the re-fitting criteria should be evaluated for corrective action. If a failure occurs in the low point and it is equivalent to the LOQ, the analyte should be reported as estimated near that concentration or the LOQ should be reestablished at a higher concentration.

11.3.6 ICV: Prior to analyzing samples, verify the ICAL using a standard obtained from a second source to the calibration standard, if possible, such as a second manufacturer or a manufacturer's batch prepared independently from the batch used for calibration, if readily available. This standard should be prepared in the same clean control matrix as that used for ICAL standards. Suggested acceptance criteria for the analyte concentrations in this standard are 70 - 130% of the expected analyte concentration(s). Quantitative sample analyses should not proceed for those analytes that do not meet the ICAL verification criteria.

11.4 CCV: A CCV standard must be analyzed at the beginning of each twelve-hour analytical period prior to any sample analysis.

NOTE: Tune checks (Sec. 11.3.1) are only required prior to ICAL.

11.4.1 The ICAL function (Sec. 11.3) for each compound of interest must be verified once every twelve hours prior to sample analysis, using the same introduction technique and conditions as used for analysis of ICAL standards and samples. This is accomplished by analyzing a CCV standard (containing all the compounds that will be reported) prepared from the same stock solutions or source materials used for ICAL standards and at a concentration near the midpoint of the ICAL range. The results must be compared against the most recent calibration curve and should meet the CCV acceptance criteria provided in Secs. 11.4.3-11.4.5.

NOTE: This QC check may be omitted if samples are analyzed within twelve hours of ICAL, and injection of the last ICAL standard may be used as the starting time reference for evaluation. A blank must also be analyzed after the CCV standard and prior to any samples in order to demonstrate that the total system (introduction device, transfer lines and GC/MS system) is free from contaminants. Analytes of interest that did not meet the criteria should be identified to the data user and results qualified appropriately. If the blank indicates contamination, then it may be appropriate to analyze additional blanks to reduce any system contamination due to carryover from standards or samples.

11.4.2 CCV standard criteria

11.4.2.1 The calculated concentration or amount of each analyte of interest in the CCV standard should fall within ±20% of the expected value.

NOTE: For the RF calibration model, % difference between the calculated RF of an analyte in the calibration verification standard and the RFavg of that analyte from the ICAL is the same value as % drift for calculated vs. expected concentration.

11.4.2.2 If the % difference or % drift for a compound is ≤ 20%, then the ICAL for that compound is assumed to be valid. Due to the large number of compounds

that may be analyzed by this method, it is likely that some compounds will not meet this criterion. If the criterion is not met (i.e., greater than 20% difference or drift) for more than 20% of the compounds included in the ICAL (or more than 20% of those that will be reported), then corrective action must be taken prior to analysis of samples. In these cases, the affected target analytes may still be reported as non-detects in samples if it can be demonstrated that there was adequate sensitivity to detect the compound at the applicable quantitation limit. For situations when the failed compound is measured in samples, the reported concentrations must be qualified appropriately.

11.4.2.3 Problems similar to those listed under ICAL could affect the ability to pass the CCV criteria. If the problem cannot be corrected by other measures, a new ICAL must be generated. The calibration verification criteria must be met before sample analysis begins.

11.4.3 IS-RT: If the absolute RT for any IS changes by more than 30 seconds from that in the mid-point standard level of the most recent ICAL sequence, then the chromatographic system must be inspected for malfunctions and corrections must be made, as required. When corrections are made, reanalysis of samples analyzed while the system was malfunctioning is required.

11.4.4 IS responses: In order to demonstrate continued stability of the measurement system after ICAL, IS responses in the CCVs must be evaluated by comparing them to the responses of the same ISs in the ICAL standard(s). If the response of an IS changes by more than a factor of 2 (50 - 200%) relative to the response of that IS in the mid-point ICAL standard or the average of responses in the suite of ICAL standards (as defined in the laboratory's SOP), then corrective actions should be taken. These corrective actions may include but are not limited to replacing and/or reanalyzing the CCV standard or retuning the MS and re-calibrating the instrument. When IS responses do not meet these criteria, system sensitivity may have been compromised, and sample reanalysis is recommended, especially if any action limits for the project are near the LOQ.

11.5 GC/MS analysis of samples

11.5.1 It is highly recommended that samples be screened to minimize contamination of the GC/MS system or sample introduction device from unexpectedly high concentrations of organic compounds.

When used only for screening purposes, the QC requirements in the methods above may be reduced as appropriate. Sample screening is particularly important when trying to achieve low quantitation levels.

11.5.2 Add appropriate volumes of the surrogates spiking solution and the IS spiking solution to each sample and all associated QC samples either manually or by an autosampler to achieve the desired concentrations. The surrogates and ISs may be mixed and added as a single spiking solution.

11.5.3 Add an aliquot of the target compounds spiking solution (Sec. 7.12) to any sample aliquot(s) chosen for matrix spiking. Follow the same procedure in preparing the LCS, adding the spike to the same clean control material used for calibration

standards preparation.

11.5.4 Introduce samples and associated QC samples to the GC/MS under the same conditions used for analysis of ICAL standards. When screening results indicate high levels of target analytes and/or interferences, or if analyte concentrations are measured above the calibration range, prepare and analyze an appropriate dilution of the sample(s), or choose a preparation method that is more amenable to making dilutions. Dilutions should be targeted so the response of the major constituents (previously saturated peaks) falls near the middle of the calibration range.

11.5.5 When the concentration of a compound in the sample is high enough to result in significant carryover to subsequent samples (Sec. 9.5), this analysis should be followed by at least one MB or instrument blank to demonstrate lack of carryover to the proceeding sample. If analysis of one or more blanks is not sufficient to return the system to acceptable operating conditions, more extensive decontamination procedures may be required, and subsequent recalibration may be necessary. Alternatively, when analysis of a blank is not possible prior to the next sample, such as when an unattended autosampler is employed, the analyst should review the results for at least the next sample after the high-concentration sample. If analytes in the high-concentration sample are not present in the subsequent sample, then the lack of carryover has been demonstrated. IS responses and RTs should be monitored in all samples and associated QC samples in order to provide sample-specific QA of proper analyte introduction to the GC/MS system and to anticipate the need for system inspection and/or maintenance. If the response of the primary m/z for any of the ISs in the samples or associated QC samples varies by more than a factor of two (−50% to +100%) from that of the same IS in the mid-point ICAL standard, average of ICAL standards, or most recently analyzed CCV standard (as defined in the laboratory's SOP), corrective action should be taken. Any affected samples and associated QC samples should be re-analyzed, or the associated data should be qualified.

11.6 Analyte identification

11.6.1 Qualitative identification of each compound determined by this method is based on RT and on comparison of the sample mass spectrum, after background correction, with a reference mass spectrum. Compounds are identified as present when the following criteria are met.

11.6.1.1 The intensities of the characteristic ions of a compound maximize in the same mass spectra or in adjacent mass spectra.

11.6.1.2 The RT is within ±10 seconds of the RT for this analyte in the midpoint ICAL standard or CCV standard analyzed at the beginning of the 12- hour period (delta RT 0.17 minute), or within ±10 seconds relative to the shift of the associated IS (delta RT of the IS ±10 seconds). Chromatograms should be carefully inspected to minimize the occurrence of both false positive and false negative results. If the RT for the IS has shifted, the sample should be inspected for similar shifts for the associated target analytes. If RT drift is significant, relative retention time (RRT) may be useful as an alternative to delta retention times.

NOTE: Some analytes may have RT shifting that is much greater than the associated IS (greater than ±10 seconds relative to the IS shift) and is still the target analyte. In those cases, it may be more useful to compare the delta RT with compounds that have similar chemistries to help identify the target. Also, dilutions or spiked samples are recommended to help determine the effects of matrix on the elution of the target and assist in target identification.

11.6.1.3 The relative intensities of the characteristic ions should agree within 30% of the intensities of these ions in the reference spectrum. For example, for an ion with an abundance of 50% in the reference spectrum, the corresponding abundance in a sample spectrum can range between 20% and 80%. The reference mass spectrum used for this comparison must be generated by the laboratory using the conditions of this method (typically from a calibration standard). Qualitative identification of sample mass spectra not acquired in limited ion acquisition modes (i.e., SIM or SRM) may also be supported by comparison to a reference library as described in Sec. 11.6.2.

11.6.1.4 Unresolved structural isomers with similar mass spectra are identified as isomeric pairs. Isomers are considered resolved if the peaks are at least 50% resolved (i.e., the height of the valley between two isomer peaks is ≤ 50% of the average of the two peak heights, or 1−[valley height]/[average peak height] is ≥ 50%). The resolution should be verified on the mid-point concentration of the ICAL as well as the laboratory-designated CCV level if closely eluting isomers are to be reported.

11.6.1.5 Identification is hampered when sample components are not resolved chromatographically and produce mass spectra containing ions contributed by more than one analyte. When gas chromatographic peaks obviously represent more than one sample component (i.e., a broadened peak with shoulder(s) or a valley between two or more maxima), appropriate selection of analyte spectra and background spectra is important.

11.6.1.6 Examination of EICPs of appropriate ions can aid in the selection of spectra, and in qualitative identification of compounds. When analytes co-elute (i.e., only one chromatographic peak is apparent), the identification criteria may be met, but each analyte spectrum will contain extraneous ions contributed by the co-eluting compound.

11.6.2 For samples containing components not associated with the calibration standards, a library search may be made for the purpose of tentative identification. The necessity to perform this type of identification will be determined by the purpose of the analyses being conducted. Data system library search routines should not use normalization routines that would misrepresent the library or unknown spectra when compared to each other. For example, the RCRA permit or waste delisting requirements may require the reporting of non-target analytes. Only after visual comparison of sample spectra with library search results may the analyst assign a tentative identification. Use the following guidelines for making tentative identifications:

11.6.2.1 Major ions in the library reference spectrum (ions greater than 10% of the most abundant ion) are present in the sample spectrum at similar relative intensities.

11.6.2.2 The molecular ion in the library reference spectrum is present in the sample spectrum. If the molecular ion is not present, carefully review library matches in order to avoid misidentification.

11.6.2.3 Major ions present in the sample spectrum but not in the reference spectrum are reviewed to determine whether they may be contributed by co-eluting compounds.

11.6.2.4 Ions present in the reference spectrum but not in the sample mass spectra are reviewed for unintended subtraction. Data system library reduction programs can sometimes create these discrepancies.

11.7 Mass spectral library search algorithms typically assign a match factor to the peak identity based on comparison of an unknown mass spectrum to library spectra. For spectra meeting the above conditions, match factors greater than 0.8 (80%) may be considered confirming evidence. Where a known limitation in data collection is identified (e.g., the presence of an incompletely resolved spectral interference), a lower match factor may be considered confirmatory. For multiple library spectra with similar match factors (e.g., for hydrocarbons with low abundance molecular ions, or structural isomers), the tentative identification assigned to the unknown may be better represented as a more generic structure (e.g., unknown hydrocarbon, C4 benzene structural isomer).

11.8 Quantitation

11.8.1 Once a compound has been identified, the quantitation of that compound will be based on the integrated abundance from the EICP of the primary characteristic ion. The IS used should be the one nearest the RT of that of a given analyte.

11.8.1.1 Where the integration produced by the software is acceptable, it is recommended to use it, because the software should produce more consistent integrations. Manual integrations are necessary when the software does not properly integrate peaks, such as when the baseline selection is improper; the correct peak is missed; a co-elution is integrated; the peak is partially integrated; etc. The analyst is responsible for ensuring that the integration is correct whether performed by the software or done manually.

11.8.1.2 Manual integrations should not be substituted for proper maintenance of the instrument or setup of the method (e.g., RT updates, integration parameter files, etc.). The analyst should seek to minimize manual integration by properly maintaining the instrument, updating RTs, and configuring peak integration parameters.

11.8.2 If the RSD is 20% or less, then the RF calibration model is acceptable for the ICAL (Sec. 11.3.4).

11.8.3 Structural isomers that produce very similar mass spectra may be quantitated as individual isomers if they are sufficiently resolved. See Sec. 11.6.1.4.

## 12.0 Data Analysis and Calculations

See Sec. 11.7 for information on data analysis and calculations.

## 13.0 Method Performance

13.1 Performance criteria should be established during validation, and the laboratory should establish in-house QC performance criteria for the application of this method. These performance data are not intended to be and must not be used as absolute QC acceptance criteria for purposes of laboratory accreditation. QC performance criteria must be established through validation of each lot.

## 14.0 Pollution Prevention

14.1 Pollution prevention encompasses any technique that reduces or eliminates the quantity and/or toxicity of waste at the point of generation. Numerous opportunities for pollution prevention exist in laboratory operations. The EPA has established a preferred hierarchy of environmental management techniques that places pollution prevention as the management option of first choice. Whenever feasible, laboratory personnel should use pollution prevention techniques to address their waste generation. When waste cannot be feasibly reduced at the source, the Agency recommends recycling as the next best option.

14.2 For information about pollution prevention that may be applicable to laboratories and research institutions consult: Less is Better: Laboratory Chemical Management for Waste Reduction available from the American Chemical Society's Department of Government Relations and Science Policy, 1155 16th St., N.W. Washington, D.C. 20036, (202) 872-4477.

## 15.0 Waste Management

The EPA requires that laboratory waste management practices be conducted consistent with all applicable rules and regulations. The Agency urges laboratories to protect the air, water, and land by minimizing and controlling all releases from hoods and bench operations, complying with the letter and spirit of any sewer discharge permits and regulations, and by complying with all solid and hazardous waste regulations, particularly the hazardous waste identification rules and land disposal restrictions. For further information on waste management, consult The Waste Management Manual for Laboratory Personnel available from the American Chemical Society.

## 16.0 References

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## 17.0 Acknowledgements

The above method was adapted from the EPA Method 8260D Volatile Organic Compounds by GC/MS for the Cannabis Laboratory Analysis Standards Program to meet the recommendations of the Cannabis Science Task Force as a standard method for determining residual solvents for certified cannabis laboratories in the state of Washington.

## 18.0 Tables, Diagrams, Flowcharts, and Validation Data

The following pages contain the tables and figures referenced by this method.

Table 1: Characteristic masses (m/z) for residual solvent compounds.

| Solvent | CAS # | Primary Ion | Secondary Ion(s) |
|---|---|---|---|
| Acetone | 67-64-1 | 43 | 58 |
| Benzene | 71-43-2 | 78 | 51,77 |
| Butanes (Sum of Isomers) | | | |
| • n-butane | 106-97-8 | 43 | 29,58 |
| • 2-methylpropane (isobutane) | 75-28-5 | 43 | 41,27 |
| Cyclohexane | 110-82-7 | 56 | 84,59 |
| Chloroform | 67-66-3 | 83 | 85,47 |
| Dichloromethane | 75-09-2 | 49 | 84,86 |
| Ethanol | 64-17-5 | 31 | 45,29 |
| Ethyl acetate | 141-78-6 | 43 | 45,61 |
| Heptanes (Single Isomer) | | | |
| • n-heptane | 142-82-5 | 43 | 57,71 |
| Hexanes (Sum of Isomers) | | | |
| • n-hexane | 110-54-3 | 57 | 43,29 |
| • 2-methylpentane | 107-83-5 | 43 | 71,42 |
| • 3-methylpentane | 96-14-0 | 57 | 56,41 |
| • 2,2-dimethylbutane | 75-83-2 | 43 | 57,71 |
| • 2,3-dimethylbutane | 79-29-8 | 43 | 42,71 |
| Isopropanol (2-propanol) | 67-63-0 | 45 | 43,27 |
| Methanol | 67-56-1 | 31 | 32,29 |
| Pentanes (Sum of Isomers) | | | |
| • n-pentane | 109-66-0 | 43 | 57,72 |
| • methylbutane (isopentane) | 78-78-4 | 43 | 57,42 |
| • dimethylpropane (neopentane) | 463-82-1 | 57 | 41,29 |
| Propane | 74-98-6 | 29 | 44,27 |
| Toluene | 108-88-3 | 91 | 92 |
| Xylenes (Sum of Isomers) | | | |
| • 1,2-dimethylbenzene (ortho-) | 95-47-6 | 91 | 106 |
| • 1,3-dimethylbenzene (meta-) | 108-38-3 | 91 | 106 |
| • 1,4-dimethylbenzene (para-) | 106-42-3 | 91 | 106 |

Table 2: Internal standards/surrogates

| Compound | Primary Characteristic Ion | Secondary Characteristic Ion(s) |
|---|---|---|
| Benzene-*d5* | 84 | 83 |
| Bromobenzene-*d5* | 82 | 162 |
| Bromochloromethane-*d2* | 51 | 131 |
| 4-Bromofluorobenzene | 95 | 174, 176 |
| Chlorobenzene-*d5* | 117 | - |
| Chloroform-*d1* | 84 | - |
| Dibromofluoromethane | 113 | - |
| 1,2-Dichlorobenzene-d4 | 152 | 115, 150 |
| 1,4-Dichlorobenzene-*d4* | 152 | 115, 150 |
| Dichloroethane-*d4* | 102 | - |
| 1,4-Difluorobenzene | 114 | - |
| Fluorobenzene | 96 | 77 |
| Pentafluorobenzene | 168 | - |
| Toluene-*d8* | 98 | - |
| 1,1,2-Trichloroethane-*d3* | 100 | - |

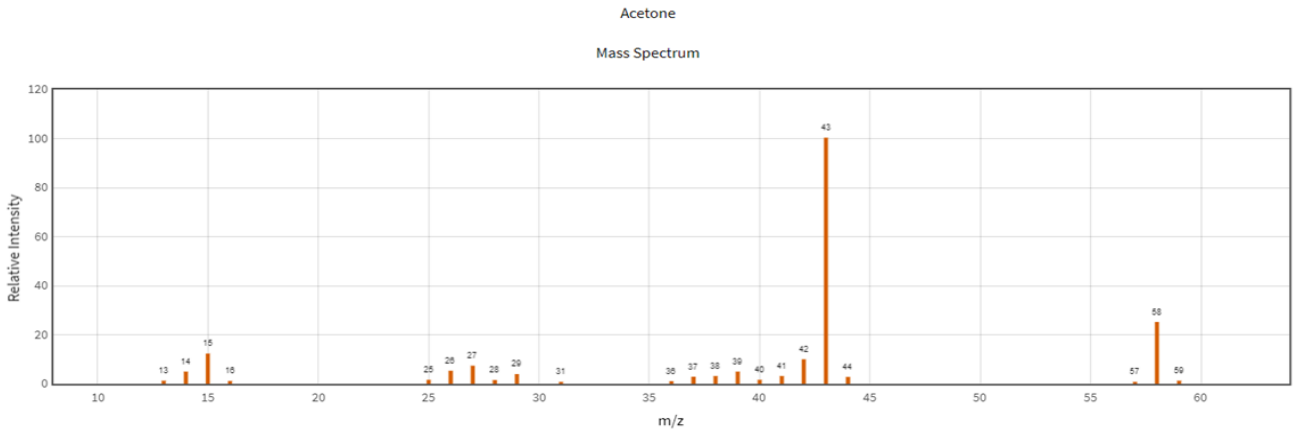
*Characteristic ion for an ion trap MS (to be used when ion-molecule reactions are observed).

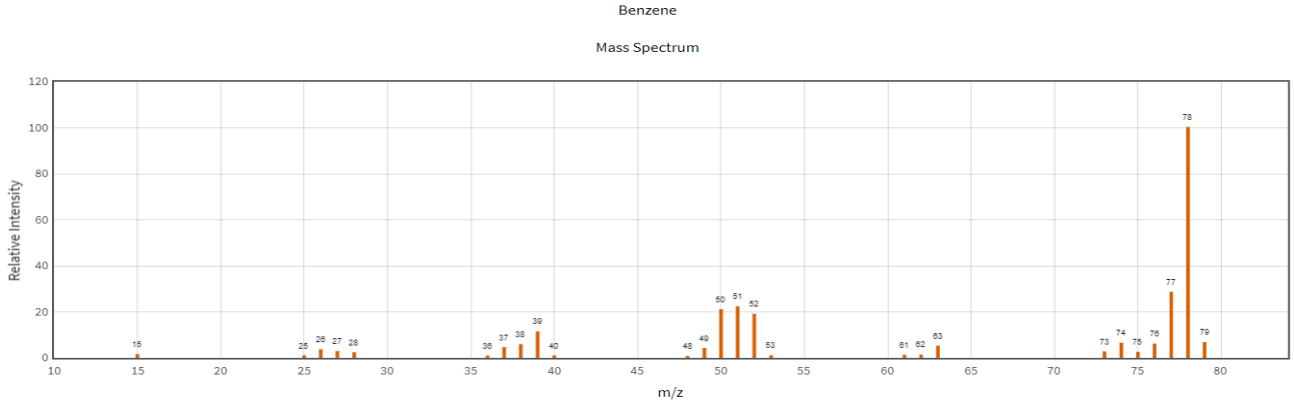
Table 3: Summary of QC criteria for use with GC/MS Method.

| Quality Control Type | Minimum frequency | Specification | Suggested Acceptance Criteria |
|---|---|---|---|
| Instrument performance check (Secs. 9.3, 11.3.1) | Prior to initial calibration | Must be verified prior to initial calibration | Meet ion ratio criteria for reference compound: 4-Bromofluorobenzene, or Perfluorotributyamine (PFTBA), or alternative documented criteria |
| Initial Calibration (ICAL) (Secs. 9.2.2, 11.3.2-11.3.5) | Prior to analyzing samples, and as needed if continuing performance criteria cannot be met | 5 points minimum for RF and linear regressions, 6 points minimum for quadratic regressions; >90% of reported target analytes meet initial calibration criteria | For average response factor (RF) calibration model: ≤20% RSD of RFs; For linear or quadratic regression model: $R \geq 0.997$, $R^2 \geq 0.995$; Independent of calibration model: Lower standard (LOQ) recalculation (refit) is within ±50% of true value; Other standards > LOQ are within ±30% of true value; Or, relative standard error (RSE) ≤20%. |
| ICAL Verification (ICV) (Secs. 9.2.2, 11.3.6) | After each initial calibration, and prior to analyzing samples | Prepared from different source of target analytes than initial calibration standards | Calculated concentrations of target analytes are within ±30% of expected value |
| Continuing Calibration Verification (CCV) (Secs. 9.2.3, 11.4) | Once every 12 hours | >80% of target analytes meet continuing calibration verification criteria | Target analytes and surrogates are ≤20% difference or drift; internal standard responses are within 50% to 200% of mid-point of ICAL or average of ICAL internal standards; and retention times for internal standards have not shifted > 30 seconds relative to ICAL |
| Blanks (Secs. 9.4, 9.5.1) | One method blank per preparation batch of 20 or fewer samples; instrument blanks as needed | NA | Target analyte concentrations in blanks are < 1/2 LOQ, or ≤ 10% of concentration in samples |
| Laboratory Control Standard (LCS) (Sec 9.5.2) | One per preparation batch of 20 or fewer samples | NA | Meets recovery criteria (CCV criteria may be used if LCS and CCV are identical) |
| Duplicates and Matrix Spikes (Secs. 9.5.3) | A duplicate and matrix spike, or matrix spike/matrix spike duplicate per preparation of 20 or fewer samples (not required per batch) | NA | Meets performance-based or project-defined recovery criteria and for relative % difference between sample and laboratory duplicate or matrix spike/matrix spike duplicate; |

| Quality Control Type | Minimum frequency | Specification | Suggested Acceptance Criteria |
|---|---|---|---|
| Surrogates (Secs. 9.6) | Added to each sample | NA | Meets performance-based recovery criteria established by the laboratory or criteria chosen for the project |
| Internal Standards (Secs. 9.7) | Added to each sample | NA | Internal standard response is within 50-200% of the response of the same internal standard in the midpoint ICAL standard (or average of ICAL) or most recent CCV |
| Qualitative Analyte Identification (Sec. 11.6.1) | Each target analyte | NA | RT in sample is within ±10 sec of RT in midpoint ICAL or CCV standard<br>Characteristic ion(s) are within ±30% of expected ion ratio in reference spectrum; or, match to reference library spectra ≥0.8 (only for full mass range acquisition modes) |

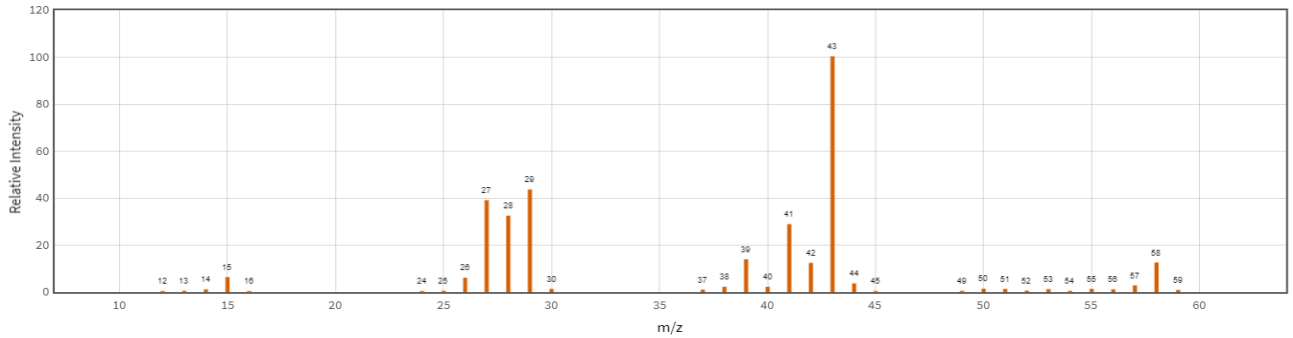
## Appendix A: Mass Spectrum of Residual Solvents



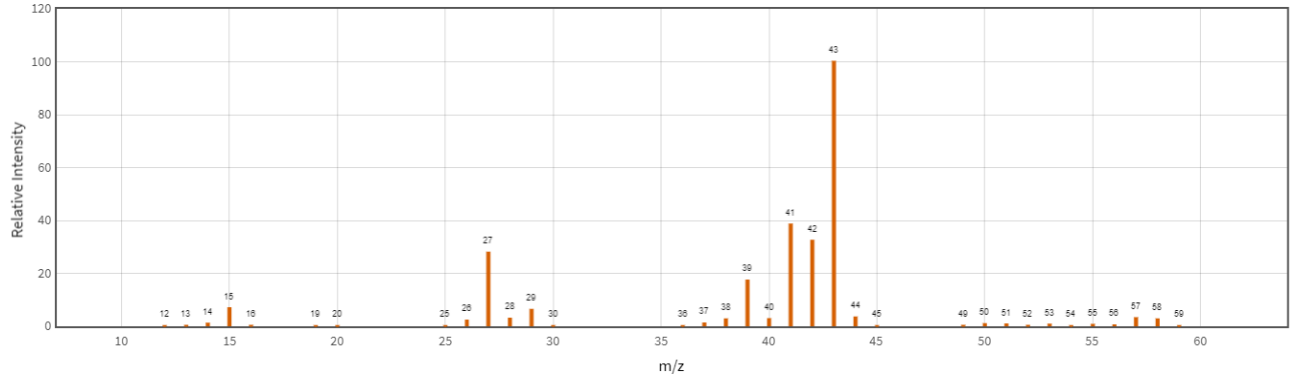
Butane

Mass Spectrum



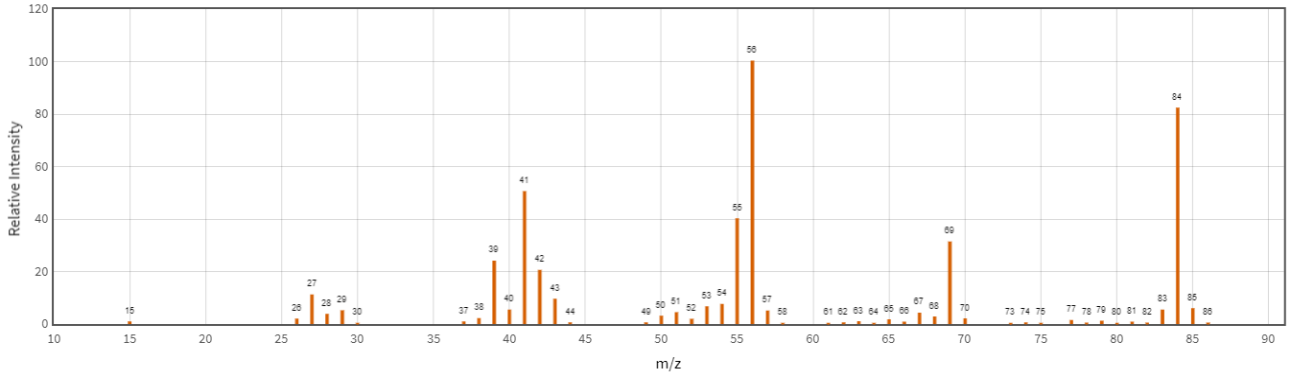

Isobutane

Mass Spectrum



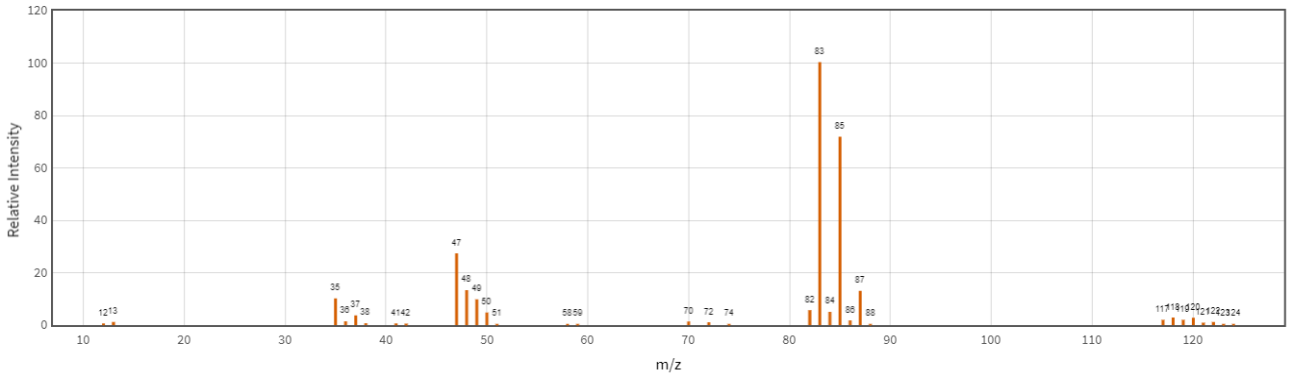

Cyclohexane

Mass Spectrum



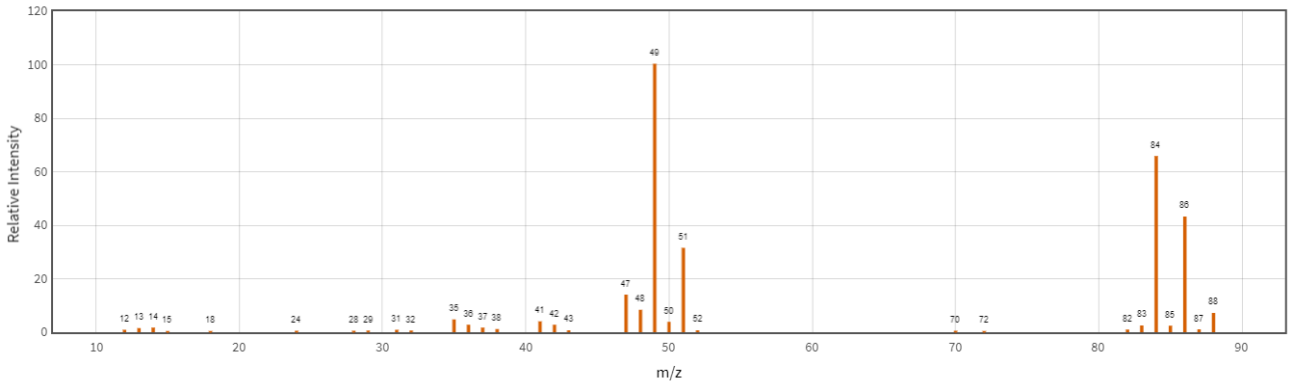
Trichloromethane

Mass Spectrum



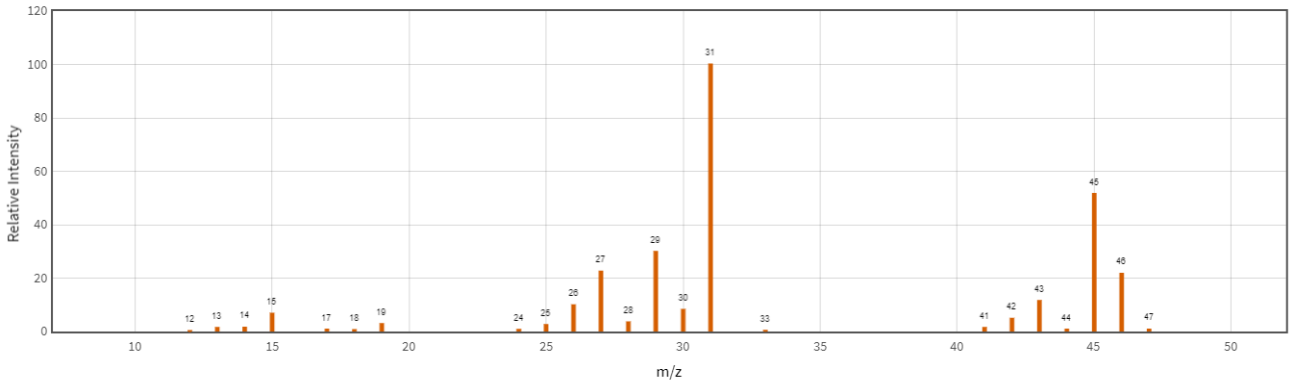

Methylene chloride

Mass Spectrum



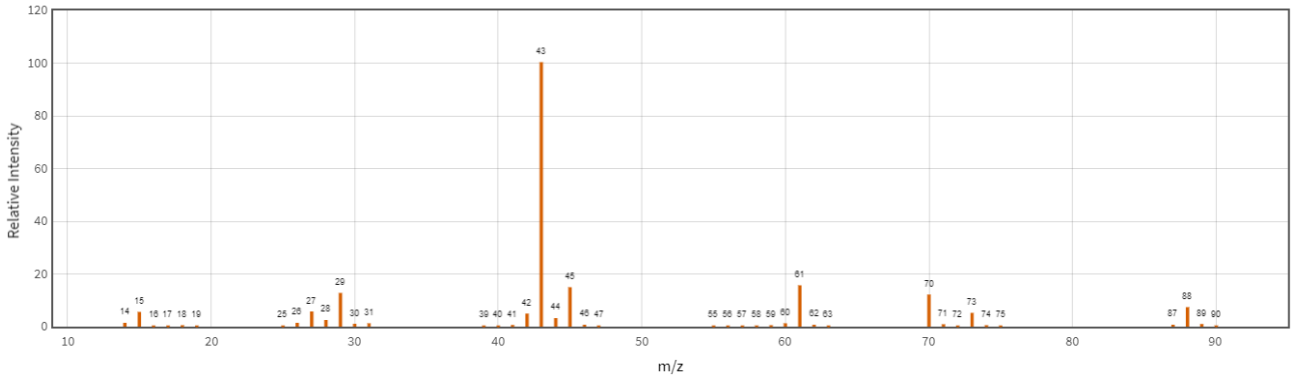

Ethanol

Mass Spectrum



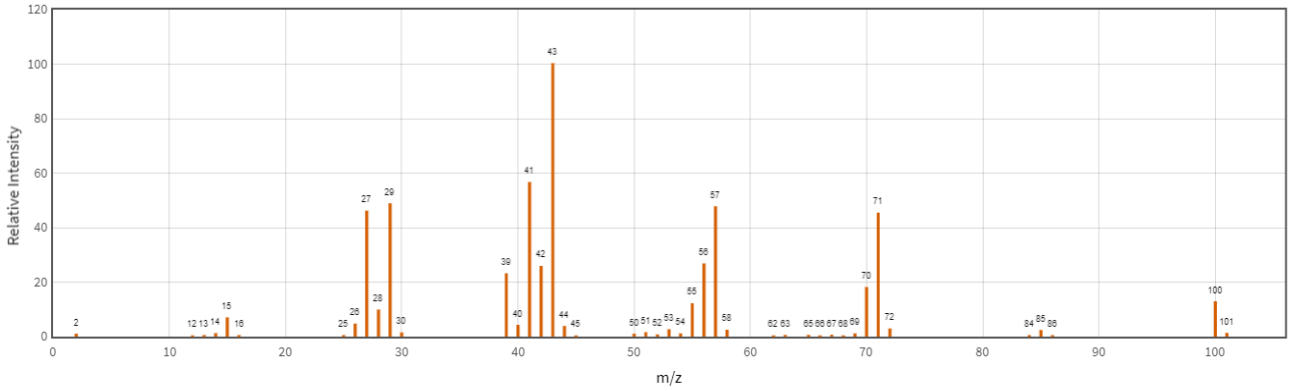
Ethyl Acetate

Mass Spectrum



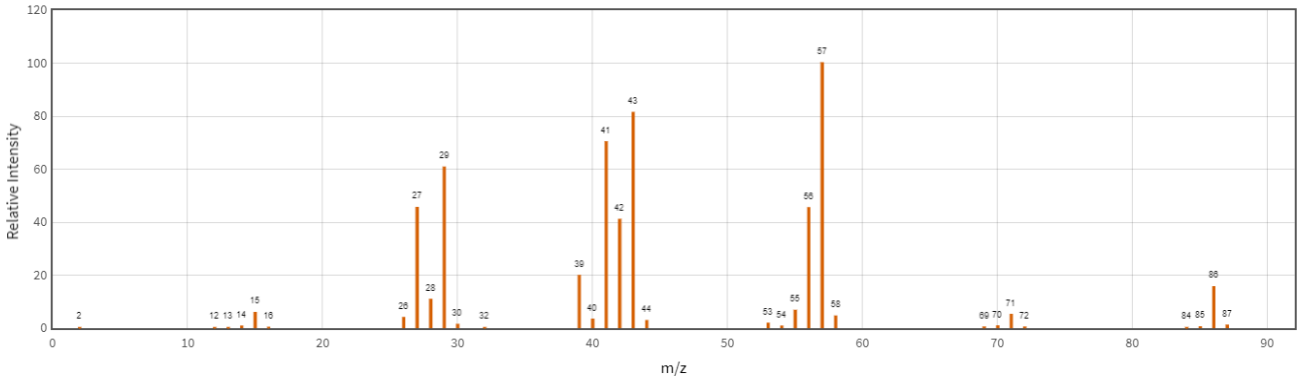

Heptane

Mass Spectrum



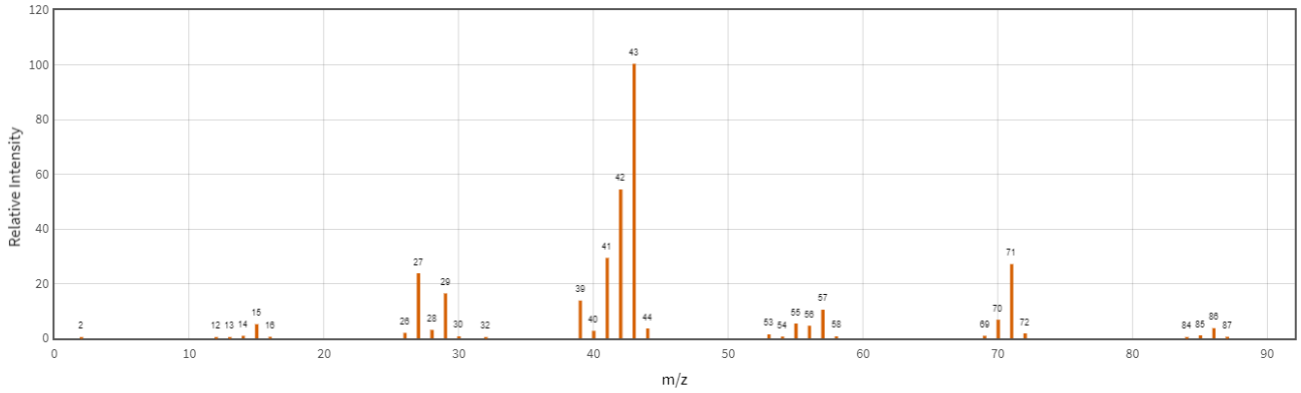

n-hexane

Mass Spectrum



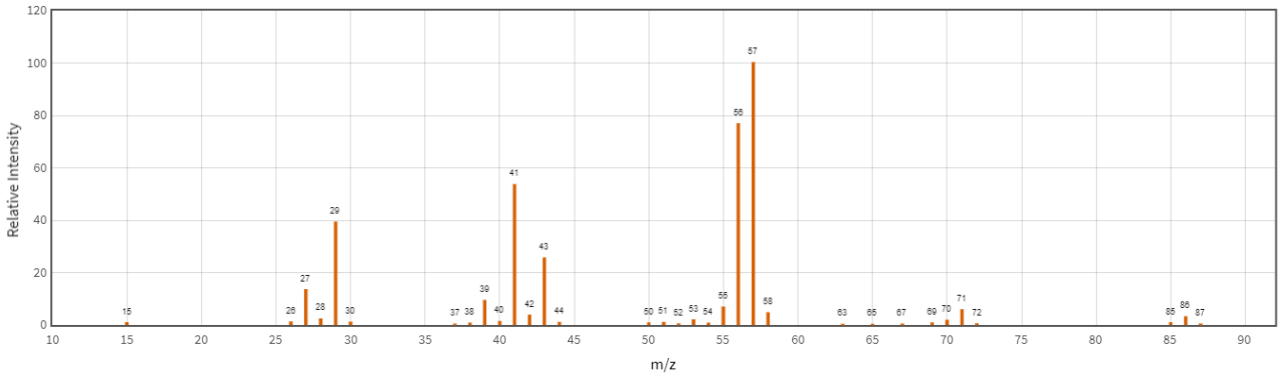
Pentane, 2-methyl-

Mass Spectrum



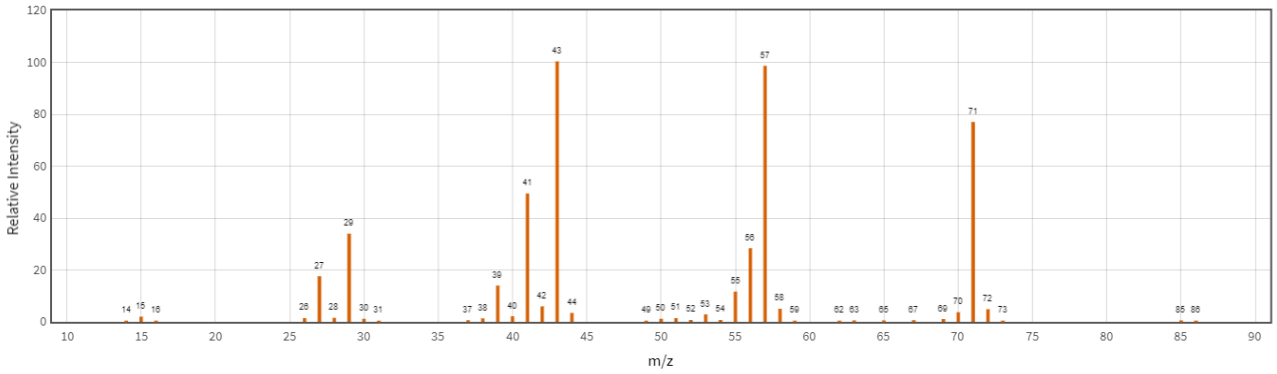

Pentane, 3-methyl-

Mass Spectrum



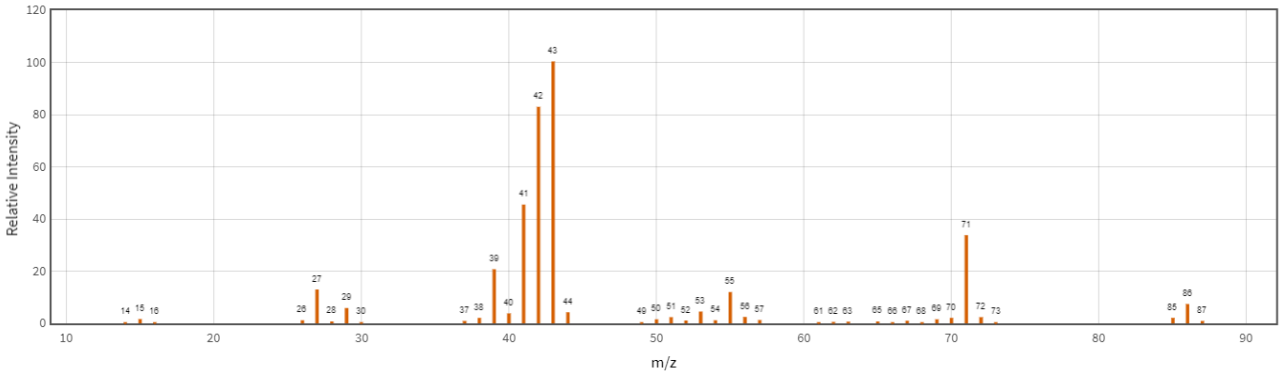

Butane, 2,2-dimethyl-

Mass Spectrum



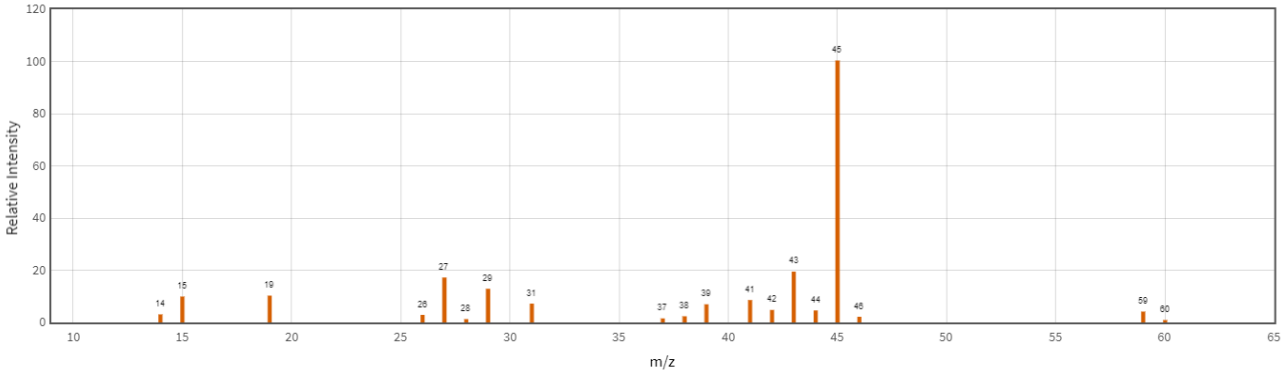
Butane, 2,3-dimethyl-

Mass Spectrum



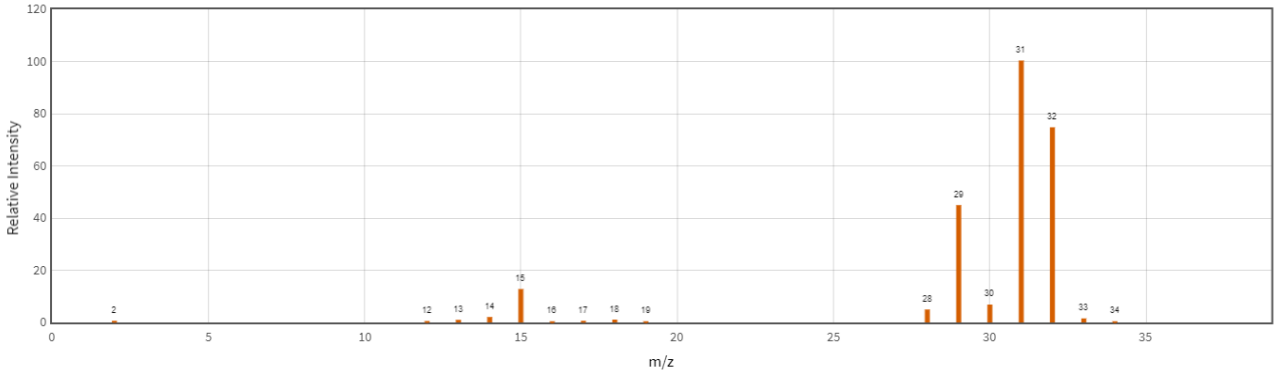

Isopropyl Alcohol

Mass Spectrum



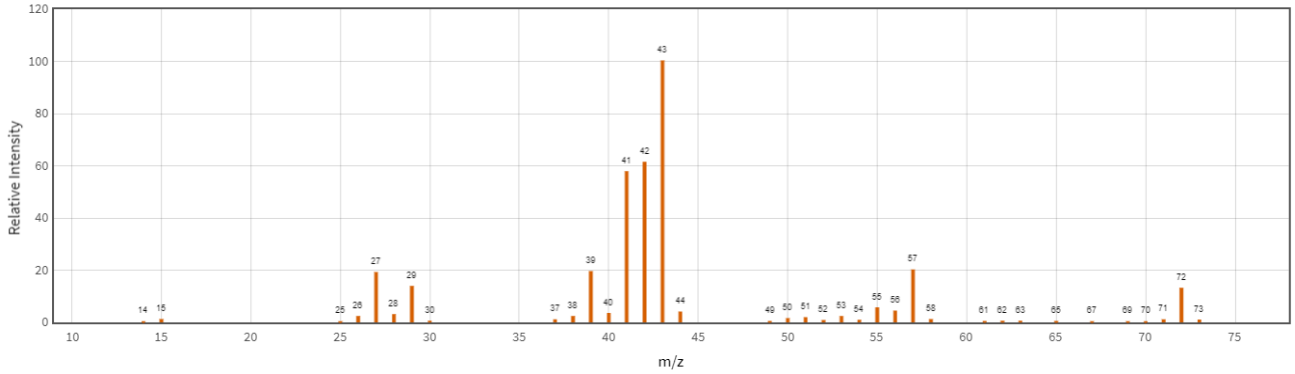

Methyl Alcohol

Mass Spectrum



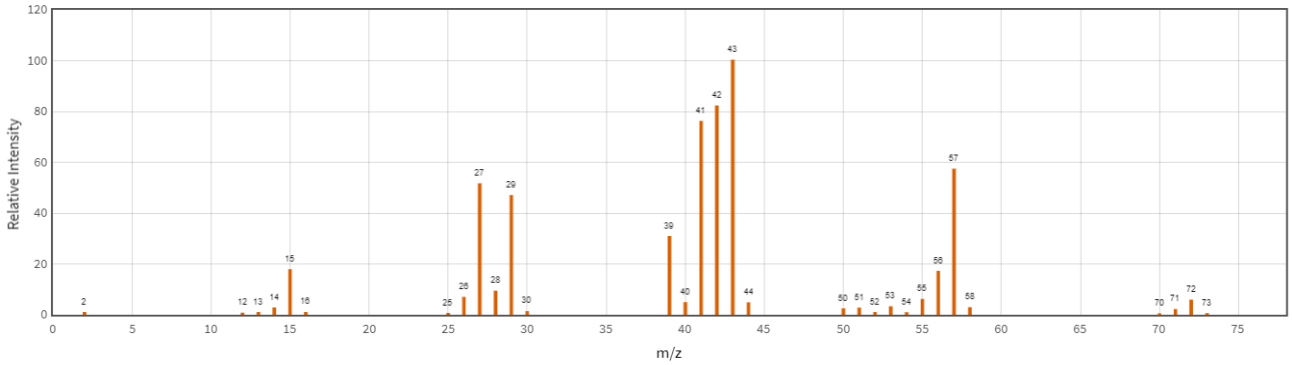
Pentane

Mass Spectrum



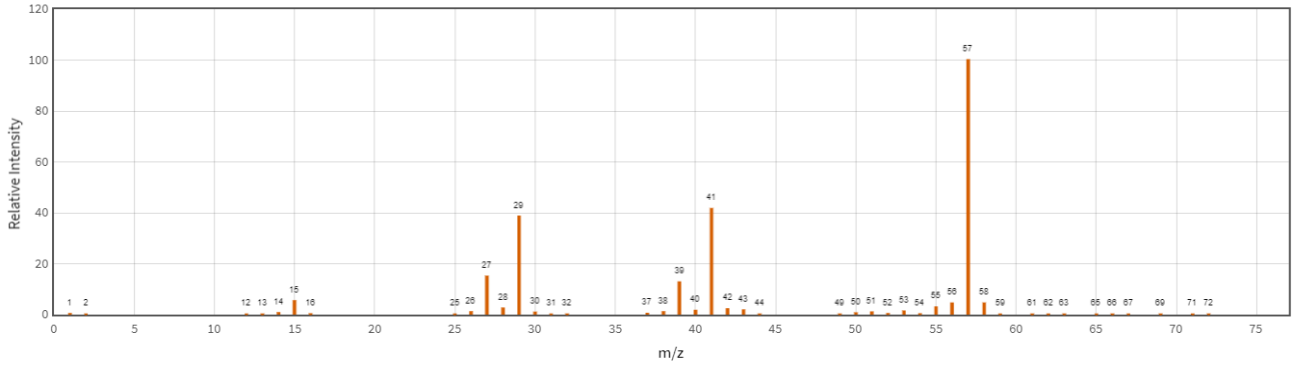

Butane, 2-methyl-

Mass Spectrum



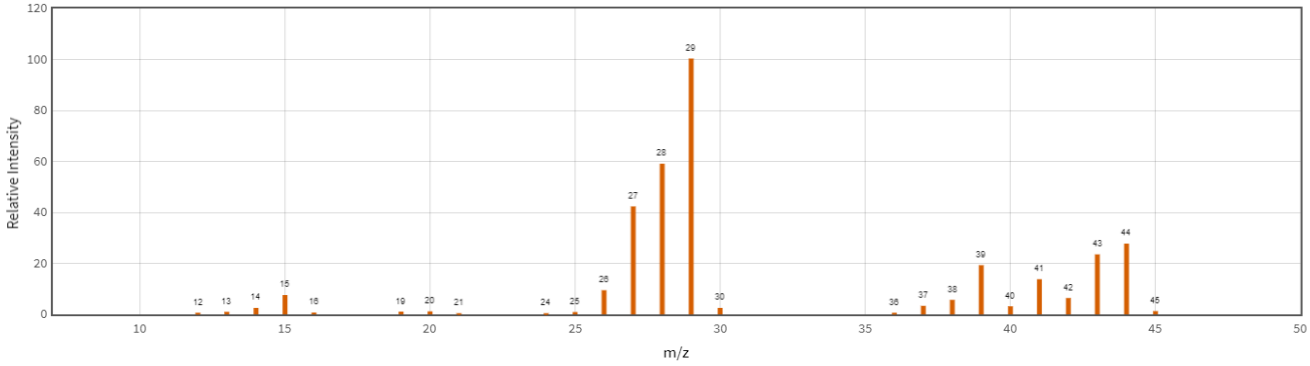

Neopentane

Mass Spectrum



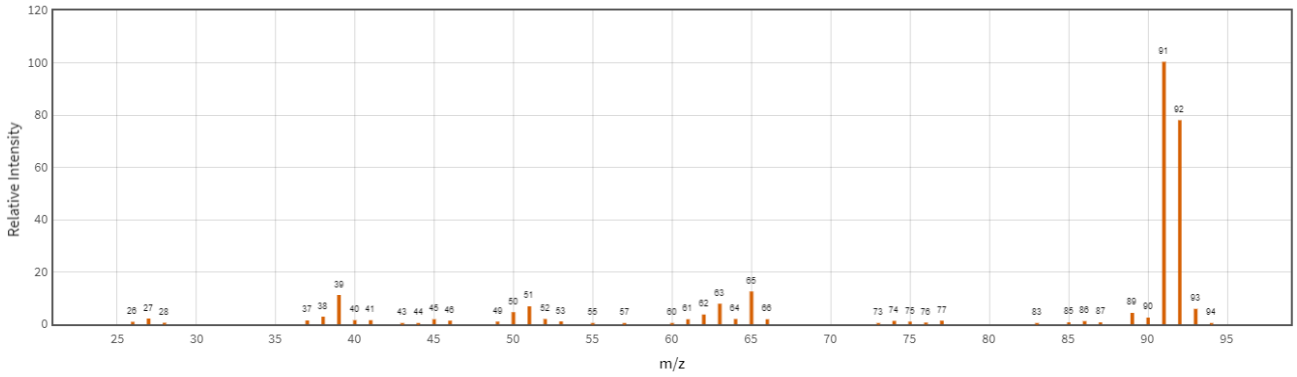
Propane

Mass Spectrum



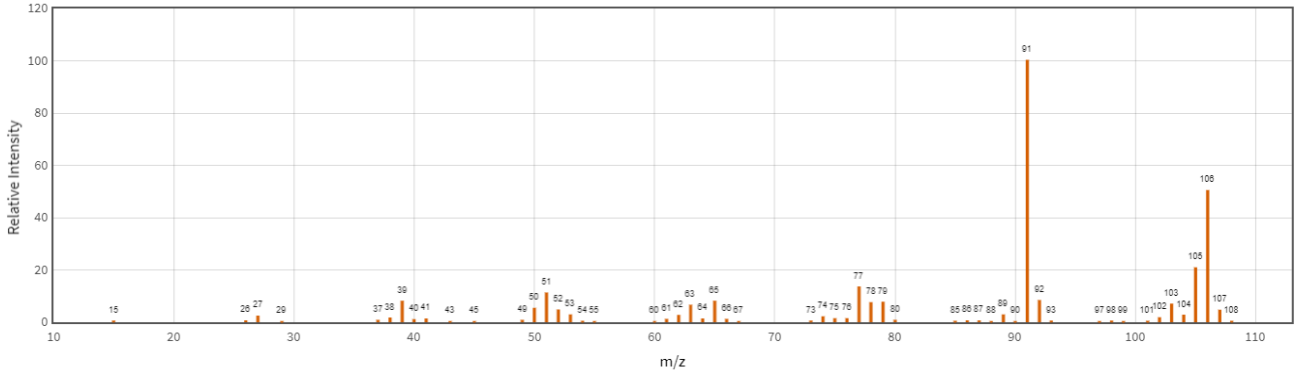

Toluene

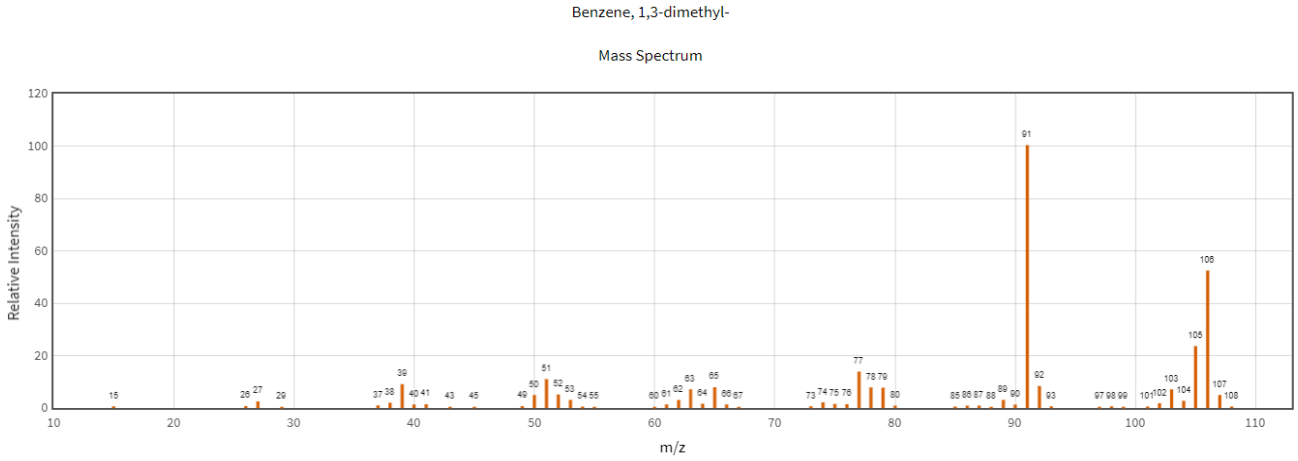
Mass Spectrum

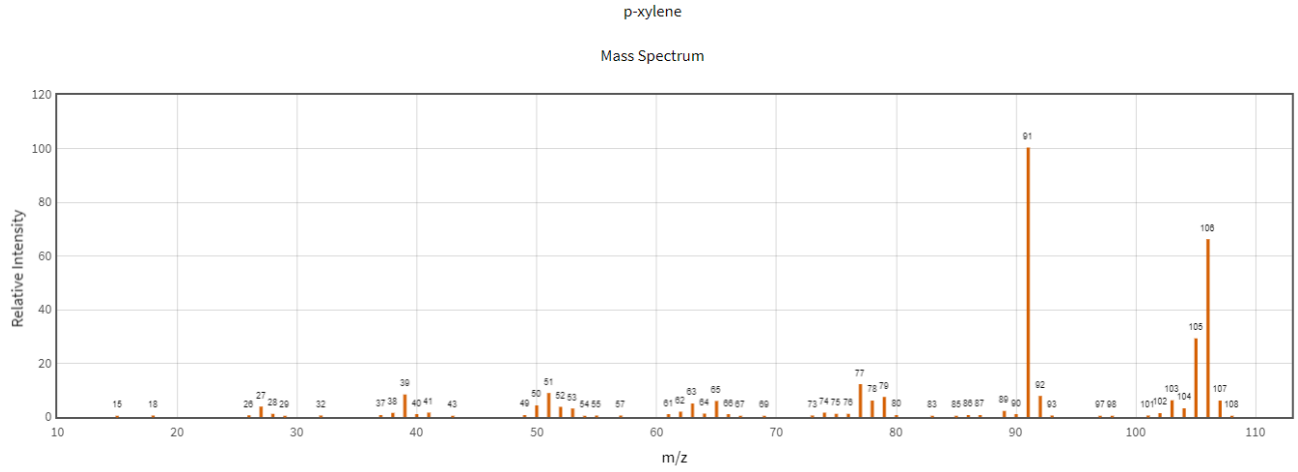



o-xylene

Mass Spectrum






## Appendix B: Guidance for Using Hydrogen Carrier Gas

B1.0 Guidance for Using Hydrogen Carrier Gas

B1.1 Hydrogen is an acceptable carrier gas to use for this analysis. However, the following modifications may be needed to make the analysis comparable to helium carrier gas:

B1.1.1 It is recommended that the highest purity (99.999% or better) hydrogen gas be used, such as from a generator or from high purity cylinders that will have minimal interferences present (e.g., hydrocarbons and water). Use of stainless steel tubing instead of copper tubing may increase the longevity of gas lines as older copper lines may become brittle over time with the use of hydrogen. MS ion source materials should be designed and approved for use with hydrogen. Contact the manufacturer of the MS to confirm the ion source is compatible with hydrogen.

Additionally, the pressure in the source should be reduced when hydrogen is used to prevent chemical ionization or other detrimental reactions from occurring. This may be done by the use of narrower bore columns (0.18 mm ID or smaller), reduction in the flow to the MS, and/or by the use of internal MS vacuum pumps (turbo pumps) with greater volumetric or pumping efficiency. Hydrogen may not be a suitable carrier gas for systems that have internal diffusion pumps.

B1.1.2 Use of hydrogen will clean (scrub) the metal surfaces of the analytical system of compounds that have adhered to the surface, generally hydrocarbons, and increase the background presence of these interferences. A bake-out of the system using high flows of hydrogen may decrease these interferences to a level that would not interfere with analysis. It is also recommended that new filters be installed on gas lines (or remove them altogether if gas purity is sufficient) to prevent the scrubbing of impurities from the filters.

B1.2 Use of hydrogen as the carrier gas may also reduce the responses of target analytes (i.e., approximately 2 - 5 times) as compared to helium. RF criteria listed in Table 4 were developed using helium carrier gas and are not appropriate for hydrogen carrier gas due to the reduced response of some analytes. If minimum RFs are used in evaluating the calibration, the laboratory should develop their own criteria or use published RFs from the instrument manufacturer. Reactivity of target analytes will vary with instrument conditions. As part of the demonstration of capability (DOC) process, evaluate target analytes for stability under the expected analytical conditions.

B1.3 As with any method modification, all QC procedures listed in Sec. 9.0 of this method should be repeated and passed using hydrogen as the carrier gas prior to the analysis of samples. Use of alternate solvents for calibration standards and extracts would also require repeating these QC procedures prior to analysis of samples.

B1.4 Hydrogen gas is highly flammable and additional safety controls may be necessary to prevent explosive levels of gas from forming. This may be accomplished by connecting vent lines from the GC inlet and MS rough pump to exhaust systems in the laboratory and leak testing all gas line connections. The flow of hydrogen should also be turned off at the source prior to opening gas lines on the GC and prior to venting the MS (such as when maintenance is performed). The user should consult additional guidelines for the safe use of hydrogen from the instrument manufacturer prior to implementing its use.